## **WEST Search History**

DATE: Sunday, December 15, 2002

Set Name side by side	Query	Hit Count	Set Name result set
DB = USPT, PO	GPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ	r	
L13	6107281.pn.	2	L13
L12	110 and L11	12	L12
L11	antimicrobial or antibacterial	104116	L11
L10	18 and L9	14	L10
L9	adhesive	773989	L9
L8	16 and L7	52	L8
L7	oral	148595	L7
L6	ascorbyl phosphate	400	L6
L5	11 and L4	1	L5
L4	polymeric.ti.	32702	L4
L3	11 and L2	6	L3
L2	3m.as.	7001	L2
L1	godbey.in.	55	L1

END OF SEARCH HISTORY

```
=> s ascorbyl 2 phosphate
            59 ASCORBYL
      14611369 2
        169107 PHOSPHATE
L1
             2 ASCORBYL 2 PHOSPHATE
                  (ASCORBYL (W) 2 (W) PHOSPHATE)
=> d l1 1-2
     ANSWER 1 OF 2 REGISTRY COPYRIGHT 2002 ACS
L1
RN
     23666-04-8 REGISTRY
     L-Ascorbic acid, 2-(dihydrogen phosphate), magnesium salt (1:1) (8CI, 9CI)
CN
     (CA INDEX NAME)
OTHER NAMES:
     Magnesium ascorbyl 2-phosphate
CN
     STEREOSEARCH
FS
MF
     C6 H9 O9 P . Mg
CI
LC
                  BEILSTEIN*, CA, CAPLUS, CHEMLIST, TOXCENTER, USPATFULL
         (*File contains numerically searchable property data)
CRN
     (23313-12-4)
```

Absolute stereochemistry.

\_,i

Mg

```
80 REFERENCES IN FILE CA (1962 TO DATE)
              80 REFERENCES IN FILE CAPLUS (1962 TO DATE)
     ANSWER 2 OF 2 REGISTRY COPYRIGHT 2002 ACS
L1
     23313-12-4 REGISTRY
RN
     L-Ascorbic acid, 2-(dihydrogen phosphate) (8CI, 9CI) (CA INDEX NAME)
CN
OTHER NAMES:
     Ascorbic acid 2-phosphate
CN
     L-Ascorbic acid 2-phosphate
CN
     L-Ascorbic acid 2-phosphate (ester)
CN
CN
     L-Ascorbyl-2-phosphate
FS
     STEREOSEARCH
DR
     172173-78-3, 81877-56-7
     C6 H9 O9 P
MF
CI
     COM
                  AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
LC
     STN Files:
       BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS, DDFU, DRUGU,
       EMBASE, IPA, MEDLINE, PROMT, TOXCENTER, USPAT7, USPATFULL, VETU
         (*File contains numerically searchable property data)
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Absolute stereochemistry.

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

248 REFERENCES IN FILE CA (1962 TO DATE)
16 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

248 REFERENCES IN FILE CAPLUS (1962 TO DATE)

=> s 3 ascorbyl 2 phosphate

11502789 3

59 ASCORBYL

14611369 2

169107 PHOSPHATE

L2 0 3 ASCORBYL 2 PHOSPHATE

(3 (W) ASCORBYL (W) 2 (W) PHOSPHATE)

=> s ascorbyl phosphate

59 ASCORBYL

169107 PHOSPHATE

L3 5 ASCORBYL PHOSPHATE

(ASCORBYL (W) PHOSPHATE)

=> d 13 1-5

L3 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2002 ACS

RN 128808-26-4 REGISTRY

CN L-Ascorbic acid, phosphate, sodium salt (9CI) (CA INDEX NAME) OTHER NAMES:

CN Ascorbic acid phosphate sodium salt

CN Sodium ascorbyl phosphate

FS STEREOSEARCH

MF C6 H8 O6 . x H3 O4 P . x Na

CI COM

SR CA

LC STN Files: BIOSIS, CA, CAPLUS, CEN, TOXCENTER, USPATFULL

CM 1

CRN 7664-38-2 CMF H3 O4 P

CM 2

CRN 50-81-7 CMF C6 H8 O6 Absolute stereochemistry.

66 REFERENCES IN FILE CA (1962 TO DATE) 66 REFERENCES IN FILE CAPLUS (1962 TO DATE)

L3 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2002 ACS

RN 128808-25-3 REGISTRY

CN L-Ascorbic acid, phosphate, potassium salt (9CI) (CA INDEX NAME)

OTHER NAMES:

CN Potassium ascorbyl phosphate

FS STEREOSEARCH

MF C6 H8 O6 . x H3 O4 P . x K

SR CA

LC STN Files: CA, CAPLUS

CM 1

CRN 7664-38-2 CMF H3 O4 P

CM 2

CRN 50-81-7 CMF C6 H8 O6

Absolute stereochemistry.

7 REFERENCES IN FILE CA (1962 TO DATE)

7 REFERENCES IN FILE CAPLUS (1962 TO DATE)

L3 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2002 ACS

RN 128808-24-2 REGISTRY

CN L-Ascorbic acid, phosphate, calcium salt (9CI) (CA INDEX NAME) OTHER NAMES:

```
Calcium ascorbyl phosphate
CN
FS
     STEREOSEARCH
     C6 H8 O6 . x Ca . x H3 O4 P
MF
SR
     STN Files: CA, CAPLUS, TOXCENTER
LC
     CM
          1
     CRN 7664-38-2
     CMF H3 O4 P
   0
      OH
HO-
   OH
     CM
          2
     CRN
         50-81-7
     CMF C6 H8 O6
Absolute stereochemistry.
                   OH
 НО
          ОН
              10 REFERENCES IN FILE CA (1962 TO DATE)
              10 REFERENCES IN FILE CAPLUS (1962 TO DATE)
     ANSWER 4 OF 5 REGISTRY COPYRIGHT 2002 ACS
L3
RN
     125913-31-7 REGISTRY
     L-Ascorbic acid, phosphate (9CI) (CA INDEX NAME)
CN
OTHER NAMES:
     Ascorbic acid phosphate
CN
     Ascorbyl phosphate
CN
     Rovimix STAY-C
CN
CN
     Rovimix STAY-C 25
     Rovimix Stay-C 35
CN
     STEREOSEARCH
FS
     C6 H8 O6 . x H3 O4 P
MF
SR
LC
     STN Files:
                  AGRICOLA, BIOBUSINESS, BIOSIS, CA, CAPLUS, IPA, TOXCENTER,
       USPATFULL
```

CM

1

CRN 7664-38-2 CMF H3 O4 P

CM 2

CRN 50-81-7 CMF C6 H8 O6

Absolute stereochemistry.

98 REFERENCES IN FILE CA (1962 TO DATE)

11 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

98 REFERENCES IN FILE CAPLUS (1962 TO DATE)

L3 ANSWER 5 OF 5 REGISTRY COPYRIGHT 2002 ACS

RN 108910-78-7 REGISTRY

CN L-Ascorbic acid, phosphate, magnesium salt (9CI) (CA INDEX NAME) OTHER NAMES:

CN Ascorbic acid phosphate magnesium salt

CN C-Mate

CN Magnesium ascorbate phosphate

CN Magnesium ascorbyl phosphate

CN Magnesium L-ascorbate phosphate

FS STEREOSEARCH

DR 224960-02-5

MF C6 H8 O6 .  $\times$  H3 O4 P .  $\times$  Mg

CI COM

SR CA

LC STN Files: BIOSIS, CA, CAPLUS, CEN, CHEMCATS, CSCHEM, TOXCENTER, USPATFULL

CM 1

CRN 7664-38-2 CMF H3 O4 P

CM 2

CRN 50-81-7 CMF C6 H8 O6

## Absolute stereochemistry.

276 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
276 REFERENCES IN FILE CAPLUS (1962 TO DATE)

=> file medicine
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 48.58 48.79

FULL ESTIMATED COST

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FILE 'USPAT2' ENTERED AT 15:04:57 ON 15 DEC 2002 CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

=> d his

L1 L2 (FILE 'HOME' ENTERED AT 15:02:18 ON 15 DEC 2002)

FILE 'REGISTRY' ENTERED AT 15:02:35 ON 15 DEC 2002

2 S ASCORBYL 2 PHOSPHATE

0 S 3 ASCORBYL 2 PHOSPHATE

L3 5 S ASCORBYL PHOSPHATE

FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CANCERLIT, CAPLUS, CEN, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, DRUGNL, DRUGU, EMBAL, EMBASE, ESBIOBASE, IFIPAT, IPA, JICST-EPLUS, KOSMET, LIFESCI, MEDICONF, MEDLINE, NAPRALERT, NLDB, PASCAL, PHARMAML, ...' ENTERED AT 15:04:57 ON 15 DEC 2002

=> s l1 or l3

18 FILES SEARCHED...

L4 1302 L1 OR L3

=> s triclosan or chlorhexidine or cetylpyridinium or domiphen L5 51801 TRICLOSAN OR CHLORHEXIDINE OR CETYLPYRIDINIUM OR DOMIPHEN

=> s strontium chloride or potassium nitrate or fluoride
28 FILES SEARCHED...

L6 528902 STRONTIUM CHLORIDE OR POTASSIUM NITRATE OR FLUORIDE

=> s tartar control agent or pyrophosphate salt or zinc citrate trihydrate or sodium hexametaphosphate or sodium tripolyphosphate

20 FILES SEARCHED...

L7 16778 TARTAR CONTROL AGENT OR PYROPHOSPHATE SALT OR ZINC CITRATE TRIHY
DRATE OR SODIUM HEXAMETAPHOSPHATE OR SODIUM TRIPOLYPHOSPHATE

=> s hydrogen peroxide or carbamide peroxide or sodium percarbonate or sodium perborate or chlorine dioxide or sodium tripolyphosphate

21 FILES SEARCHED...

L8 383624 HYDROGEN PEROXIDE OR CARBAMIDE PEROXIDE OR SODIUM PERCARBONATE
OR SODIUM PERBORATE OR CHLORINE DIOXIDE OR SODIUM TRIPOLYPHOSPHA
TE

=> d his

L1

(FILE 'HOME' ENTERED AT 15:02:18 ON 15 DEC 2002)

FILE 'REGISTRY' ENTERED AT 15:02:35 ON 15 DEC 2002

2 S ASCORBYL 2 PHOSPHATE

L2 0 S 3 ASCORBYL 2 PHOSPHATE

L3 5 S ASCORBYL PHOSPHATE

FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CANCERLIT, CAPLUS, CEN, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, DRUGNL, DRUGU, EMBAL, EMBASE, ESBIOBASE, IFIPAT, IPA, JICST-EPLUS, KOSMET, LIFESCI, MEDICONF, MEDLINE, NAPRALERT, NLDB, PASCAL, PHARMAML, ...' ENTERED AT 15:04:57 ON 15 DEC 2002

L4 1302 S L1 OR L3

L5 51801 S TRICLOSAN OR CHLORHEXIDINE OR CETYLPYRIDINIUM OR DOMIPHEN

L6 528902 S STRONTIUM CHLORIDE OR POTASSIUM NITRATE OR FLUORIDE

L7 16778 S TARTAR CONTROL AGENT OR PYROPHOSPHATE SALT OR ZINC CITRATE TR

=> s 14 and 15 and 16 and 17 and 18 L9 1 L4 AND L5 AND L6 AND L7 AND L8

=> d 19 ibib, kwic

L9 ANSWER 1 OF 1 USPATFULL

ACCESSION NUMBER: 2002:251775 USPATFULL

TITLE: Topical oral care compositions

INVENTOR(S): Montgomery, R. Eric, Monterey, MA, UNITED STATES

PATENT ASSIGNEE(S): Oraceutical LLC, Lee, MA (U.S. corporation)

NUMBER DATE

PRIORITY INFORMATION: US 2001-263884P 20010124 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: BANNER & WITCOFF, LTD., 28 STATE STREET, 28th FLOOR,

\_\_\_\_\_\_

BOSTON, MA, 02109

NUMBER OF CLAIMS: 10 EXEMPLARY CLAIM: 1 LINE COUNT: 776

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

of modern dentistry. Since the advent of **fluoride** almost 50 years ago, the incidence of tooth decay, or caries, has decreased substantially. **Fluoride** is now found in drinking water and many consumer dental products, and has won widespread acceptance as a safe and. . . in the past 20 years has further expanded the therapeutic potential of topical oral care products. Antibacterial agents, such as **triclosan**, chlorhexidene salts, **cetylpyridinium** chloride, and **domiphen** bromide have been added to topical dental products to address gingivitis, periodontitis, halitosis and caries. Tooth desensitizers, such as **potassium nitrate**, **strontium chloride** and **fluoride** salts have been successfully

chloride and fluoride salts have been successfully
employed to decrease tooth sensitivity. Tartar control agents, such as
pyrophosphate salts, zinc citrate trihydrate

, sodium hexametaphosphate and sodium

tripolyphosphate are commonly used in toothpastes and
mouthwashes to prevent the buildup of dental calculus on tooth surfaces.
Tooth whitening agents, such as hydrogen peroxide,

carbamide peroxide, sodium

percarbonate, sodium perborate,

chlorine dioxide, and sodium

 ${f tripolyphosphate}$ , have more recently been added to many dental products as auxiliary ingredients that add the perceived value of white (as. . .

SUMM . . . cancers. The term ROS encompasses free radicals (such as the hydroxyl radical, OH.) or precursors to free radicals (such as hydrogen peroxide, H.sub.20.sub.2). While it is clear that the incidence of oral cancer is much higher in individuals who smoke and/or drink. . .

SUMM . . . abrasive is desired, silica abrasives are preferred, due to their inertness to many active therapeutic ingredients, such as sources of **fluoride** ion.

SUMM [0056] One or more anticaries agents, in particular **fluoride** containing or releasing compounds, may be advantageously included in the

ascorbyl phosphate compositions. Useful anticaries agents include sodium fluoride, sodium monofluorophosphate, stannous fluoride , amine fluorides, and other fluoride containing compounds capable of increasing the resistance of mineralized tissues in the oral cavity to caries formation (tooth decay). Anticaries. . . agent may be included in the inventive ascorbyl phosphate SUMM compositions. Such compounds are well known in the art, and include triclosan, chlorhexidine (and its salts), cetylpyridinium chloride, and essential oils including menthol, eucalyptol, thymol and methyl salicylate. Antimicrobial agents may be included in the ascorbyl phosphate. . . . . precipitation of calcium phosphate at the tooth surface), it SUMM may be advantageous to add a supplementary tooth desensitizer such as potassium nitrate, potassium citrate, or strontium chloride hexahydrate in order to further alleviate tooth sensitivity. Such supplementary tooth desensitizers may be included in the ascorbyl phosphate compositions at a concentration of from about 0.1% by weight to about 10% by weight of the composition. Potassium nitrate is the preferred supplementary tooth desensitizer and is included in the composition at a concentration of from about 3% to.

DETD . . . formulated into a mouthwash including the ingredients set forth below.

Ingredient	Percent	(w/w)
Deionized water	86.190	
Glycerin	7.500	
Sodium tripolyphosphate	3.000	
Polyethylene glycol 8000	1.000	
Sodium saccharin	0.060	
Sodium benzoate	0.500	
Sodium ascorbyl-2-monophosphate	1.000	
PEG-60 hydrogenated castor oil	0.600	
Flavor		

DETD . . . to include the following ingredients.

•	
Deionized water	17.298
Sodium ascorbyl-2-monphosphate	0.500
Sodium benzoate	0.500
Sodium fluoride	0.240
Titanium dioxide	1.200
Sodium saccharin	0.400
Sorbitol (70% solution)	34.562
Glycerin	18.000
Cellulose gum	1.000
Hydrated silica (abrasive)	17.500

DETD . . . ascorbyl-2-monophosphate, also known simply as sodium ascorbyl phosphate.

Percent (w/w)

TABLE 1

Ingredient

Component	Mouthwash	Toothpaste/Gel
Water	46-99.9%	0-99.89%
Ascorbyl-2-phosphate	0.01-10%	0.01-10%
Fluoride ion (F-) source	0-4%	0-4%

Pi Hi	uxiliary active ingredient reservative umectant rtificial sweetener	0-10% 0-3% 0-30% 0-1%	0-10% 0-3% 0-70% 0-2%
DETD	[0072] Also contemplated is the inhibitor, such as a <b>fluoride</b> i of the present invention. Other those employed for tartar.	on source, in th	e compositions
DETD	staining contain an oxidizing or compound is either hydrogen per to hydrogen peroxide, such as operoxide, sodium perborate, sodium percarbonate, and others. It is peroxide is able to penetrate to (and more easily through cracks)	compound. Typical coxide, or a precent commide lium committed through intact en	ursor  ogen  amel and dentin
DETD	of pulp tissue damage by scaver hydrogen peroxide, such as the and the perhydroxyl radical (.Cobtained after hydrolysis of.	nging free-radica hydroxyl radical DOH). An addition	l degradation products of (.OH)
CLM	What is claimed is: 8. The composition of claim 1 wan anticaries agent, a tartar of, an antimicrobial agent, and a	ontrol agent	
IT <b>23313-12-4</b> 30784-77-1 109113-30-6 <b>125913-31-7</b> , Rovimix Stay-C 35 134885-32-8 143567-34-4 (topical oral care compns. contg. ascorbyl phosphate)			
	oral care or teeth or tooth or gu FILES SEARCHED 2769218 ORAL CARE OR TEETH OR T		
=> d his			
	(FILE 'HOME' ENTERED AT 15:02:18	ON 15 DEC 2002)	
L1 L2 L3	FILE 'REGISTRY' ENTERED AT 15:02: 2 S ASCORBYL 2 PHOSPHATE 0 S 3 ASCORBYL 2 PHOSPHA 5 S ASCORBYL PHOSPHATE	E	2
) 1	FILE 'ADISCTI, ADISINSIGHT, ADISN CAPLUS, CEN, DGENE, DRUGB, DRUGLA EMBASE, ESBIOBASE, IFIPAT, IPA, J MEDLINE, NAPRALERT, NLDB, PASCAL, 15 DEC 2002 1302 S L1 OR L3 51801 S TRICLOSAN OR CHLORHE 528902 S STRONTIUM CHLORIDE OF 16778 S TARTAR CONTROL AGENT 383624 S HYDROGEN PEROXIDE OR	AUNCH, DRUGMONOG2 FICST-EPLUS, KOSM PHARMAML,'  EXIDINE OR CETYLP OR POTASSIUM NITR OR PYROPHOSPHAT	, DRUGNL, DRUGU, EMBAL, ET, LIFESCI, MEDICONF, ENTERED AT 15:04:57 ON  YRIDINIUM OR DOMIPHEN ATE OR FLUORIDE E SALT OR ZINC CITRATE TR
L9 L10	1 S L4 AND L5 AND L6 AND 2769218 S ORAL CARE OR TEETH C	L7 AND L8	
=> s ] L11	l4 and 110 71 L4 AND L10		
=> s & L12	antibacterial or antimicrobial 981256 ANTIBACTERIAL OR ANTIMI	CROBIAL	

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=> s l11 and l12
 21 FILES SEARCHED...
            7 L11 AND L12
=> dup rem
ENTER L# LIST OR (END):113
DUPLICATE IS NOT AVAILABLE IN 'ADISINSIGHT, ADISNEWS, DGENE, DRUGLAUNCH,
DRUGMONOG2, KOSMET, MEDICONF, PHARMAML'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L13
             7 DUP REM L13 (0 DUPLICATES REMOVED)
L14
=> d 114 1-7 ibib, kwic
L14 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER:
                       2002:888524 CAPLUS
DOCUMENT NUMBER:
                        137:375265
                        Polymeric carrier system for delivering cosmetics and
TITLE:
                        pharmaceuticals
                        Godbey, Kristin J.; Kantner, Steven S.; Scholz,
INVENTOR (S):
                        Matthew T.
                        3M Innovative Properties Company, USA
PATENT ASSIGNEE(S):
                        PCT Int. Appl., 30 pp.
SOURCE:
                        CODEN: PIXXD2
DOCUMENT TYPE:
                        Patent
                        English
LANGUAGE:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
    PATENT NO.
                    KIND DATE
                                        APPLICATION NO. DATE
     _______
                                         ______
                                        WO 2002-US12479 20020411
     WO 2002092049 A2 20021121
        W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES,
            FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG,
            KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
            MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK,
            SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM,
            AZ, BY, KG, KZ
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
            CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
            BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     US 2002187181
                     A1 20021212
                                    US 2001-854824 20010514
                                       US 2001-854824 A 20010514
PRIORITY APPLN. INFO.:
    Adhesives
    Anti-inflammatory agents
    Antibiotics
      Antimicrobial agents
     Antiperspirants
     Bleaching agents
     Cosmetics
    Dentifrices
    Deodorants (personal)
    Dyes
     Emulsifying agents
     Flavoring materials
    Foams
    Fungicides
    Hair preparations
    Humectants
     Insect repellents
```

Nonwoven fabrics

Odor and Odorous substances

Perfumes Pigments, nonbiological Plasticizers Sunscreens Suntanning agents Textiles (polymeric carrier system for delivering cosmetics and pharmaceuticals) IT (polymeric carrier system for delivering cosmetics and pharmaceuticals teeth) 69-72-7, Salicylic acid, biological studies 58-95-7, Tocopherol acetate 124-43-6, Carbamide peroxide 1337-30-0, Sorbitan laurate 2466-09-3, 3380-34-5, Triclosan 7558-80-7, Monosodium phosphate Diphosphoric acid 7681-49-4, Sodium fluoride, biological studies 7722-84-1, Hydrogen 18472-51-0, Chlorhexidine gluconate peroxide, biological studies 128808-26-4, Sodium ascorbyl phosphate RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (polymeric carrier system for delivering cosmetics and pharmaceuticals) L14 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2002 ACS 2002:594979 CAPLUS ACCESSION NUMBER: DOCUMENT NUMBER: 137:121930 An improved in vitro method of culturing mammalian TITLE: cells for autologous cell implantation/transplantation Storgaard, Peter; Osther, Kurt INVENTOR(S): Interface Biotech A/S, Den. PATENT ASSIGNEE(S): PCT Int. Appl., 51 pp. SOURCE: CODEN: PIXXD2 DOCUMENT TYPE: Patent LANGUAGE: English FAMILY ACC. NUM. COUNT: PATENT INFORMATION: PATENT NO. KIND DATE APPLICATION NO. DATE ----\_\_\_\_\_\_ WO 2002-DK65 20020129 WO 2002061052 A2 20020808 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG DK 2001-162 PRIORITY APPLN. INFO.: A 20010131 IT Tooth (cementum; in vitro method of culturing mammalian cells for autologous cell implantation/transplantation methods) IT Alzheimer's disease Animal tissue culture Antimicrobial agents Blood serum Blood vessel

Bone marrow
Brain
Brain, disease
Camel (Camelus)
Chemotaxis
Chondrocyte
Connective tissue

Culture media Diabetes insipidus Diabetes mellitus Fibroblast Horse (Equus caballus) Human Liver Multiple sclerosis Muscle Mvoblast Neoplasm Osteocyte Pancreas Parkinson's disease Skin Temperature Transplant and Transplantation

(in vitro method of culturing mammalian cells for autologous cell implantation/transplantation methods)

(odontoblast; in vitro method of culturing mammalian cells for

## IT Tooth

ΤT

autologous cell implantation/transplantation methods)

1397-89-3, Fungizone 1405-41-0, Gentamicin sulfate 7439-95-4,

Magnesium, biological studies 7440-70-2, Calcium, biological studies

9001-12-1, Matrix metalloproteinase-1 9002-07-7, Trypsin 9004-06-2,

Neutrophil elastase 9025-26-7, Cathepsin D 9047-22-7, Cathepsin B

23313-12-4, L-Ascorbic acid 2-phosphate 56645-49-9, Cathepsin G

60616-82-2, Cathepsin L 71965-46-3, Cathepsin S 79955-99-0, Matrix

metalloproteinase-3 94716-09-3, Cathepsin K 128028-50-2, Myeloblastin

140610-48-6, Matrix metalloproteinase-10 141256-52-2, Matrix

metalloproteinase-7 145267-01-2, Matrix metalloproteinase-11

146480-35-5, Matrix metalloproteinase-2 146480-36-6, Matrix

metalloproteinase-9 161384-17-4, Matrix metalloproteinase-14

172308-17-7, Matrix metalloproteinase-15 175449-82-8, Matrix

metalloproteinase-13 182970-56-5, Matrix metalloproteinase-16

185766-51-2, Matrix metalloproteinase-20 186207-03-4, Proteinase

(in vitro method of culturing mammalian cells for autologous cell implantation/transplantation methods)

203810-08-6, Matrix metalloproteinase-17 227604-60-6, Membrane type matrix metalloproteinase 5 252351-86-3, Matrix metalloproteinase-6 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES

L14 ANSWER 3 OF 7 USPATFULL

(Uses)

ACCESSION NUMBER: 2002:251775 USPATFULL

TITLE: Topical oral care compositions

INVENTOR(S): Montgomery, R. Eric, Monterey, MA, UNITED STATES

inhibitor, TIMP 4 188364-80-9, Matrix metalloproteinase-19

PATENT ASSIGNEE(S): Oraceutical LLC, Lee, MA (U.S. corporation)

NUMBER DATE

PRIORITY INFORMATION: US 2001-263884P 20010124 (60)

10

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: BANNER & WITCOFF, LTD., 28 STATE STREET, 28th FLOOR,

BOSTON, MA, 02109

NUMBER OF CLAIMS:

EXEMPLARY CLAIM: LINE COUNT: 776

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Topical oral care compositions

Embodiments of the present invention are directed to topical AB oral care compositions including a free radical scavenging precursor compound.

SUMM [0002] The present invention relates to topical oral compositions that include a compound that generates a free radical scavenger compound to scavenge free radicals. Compounds according to the present invention include ascorbic acid precursor compounds that generate ascorbic acid when placed in the oral cavity. The present invention also relates to methods of using such compositions for preventing or curing various disease processes or symptoms of the oral cavity that are responsive to the presence of free radicals. The present invention also relates to oral care compositions that include phosphate precursor compounds that generate phosphates useful in oral care methods.

SUMM [0003] The maintenance of healthy teeth and gums has long been the goal of modern dentistry. Since the advent of fluoride almost 50 years ago, the incidence of tooth decay, or caries, has decreased substantially. Fluoride is now found in drinking water and many consumer dental products, and has. . . for large segments of the population. Innovation in the past 20 years has further expanded the therapeutic potential of topical oral care products. Antibacterial agents, such as triclosan, chlorhexidene salts, cetylpyridinium chloride, and domiphen bromide have been added to topical dental products to address gingivitis, periodontitis, halitosis and caries. Tooth desensitizers, such as potassium nitrate, strontium chloride and fluoride salts have been successfully employed to decrease tooth sensitivity. Tartar control agents, such as pyrophosphate salts, zinc citrate trihydrate, sodium hexametaphosphate and sodium tripolyphosphate are commonly used in toothpastes and mouthwashes to prevent the buildup of dental calculus on tooth surfaces. Tooth whitening agents, such as hydrogen peroxide, carbamide peroxide, sodium percarbonate, sodium perborate, chlorine dioxide, and sodium tripolyphosphate, have more recently. . . been added to many dental products as auxiliary ingredients that add the perceived value of white (as well as healthy) teeth to the consumer.

. radical, OH.) or precursors to free radicals (such as hydrogen peroxide, H.sub.20.sub.2). While it is clear that the incidence of oral cancer is much higher in individuals who smoke and/or drink alcohol, and it is tempting to assume that such oral cancer is a direct result of the oxidative stress place on the soft tissues of the oral cavity, very few approaches have yet been developed to address the problem. Most efforts to date have centered on the diagnostic techniques required to detect oral cancer at early stages, when it is most curable. A number of means for measuring oxidative stress in oral soft tissues have been developed. A number of topical and oral compositions have been proposed that comprise one or more antioxidants and claim to counteract the soft tissue effects of free.

[0005] It has also been recently discovered that a certain type of tooth staining is the result of the formation of Maillard, or non-enzymatic browning, reaction products. Maillard reaction products are generally based. . . reaction products appearing off-white to yellowish-red to the naked eye. When Maillard reaction products form on the surface of the teeth, the teeth appear to be stained. The Maillard reaction can occur when reducing sugars (such as glucose) are present in aqueous solution together with amino-functional compounds (such as amino acids or the amino-side chains of proteins). The oral cavity and, in particular, surfaces of the

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teeth that are covered with dental plaque, is an ideal
environment (moisture, glucose, proteins, and body heat together in one
locale). . .

SUMM . . . means of administering ascorbic acid to an organism or subject by means of ingestion, rather than topical application to the oral cavity (whereby conversion to free ascorbic acid occurs prior to ingestion, thereby exerting a therapeutic effect on one or more tissue surfaces of the oral cavity). The notion of oral residence time, or the amount of time a composition remains in contact with the oral cavity, is of importance in differentiating the compositions and methods of the present invention from those intended for administration by.

[0010] Considering the number of **oral** diseases or conditions that result directly or indirectly from the formation of ROS in the **oral** cavity, few attempts have been made to attenuate oxidative stress in the **oral** environment. The same cannot be said about efforts in non-**oral** skin care, where the effects of ROS on skin aging have been recognized for many years. U.S. Pat. No. 6,184,247.

. . cell turnover by as much as 23%, this increase in desquamation is greatly overshadowed by the natural turnover rates of **oral** mucosal tissues (hard palate, buccal mucosal, floor of the mouth mucosal), which are normally in a range from about 10%.

SUMM . . . unlikely that both the ascorbic acid and underivatized phosphate moieties would be released for immediate bioavailability if applied to the **oral** cavity. The **oral** toxicity of these derivatives and their topical formulations is also unknown.

SUMM . . . same formulation, of many different cosmetic and toiletry ingredients; however it is inappropriate to include such ingredients together within an **oral** composition that must, by definition, be suitable for partial ingestion by the user.

SUMM [0013] Kayane, et al (U.S. Pat. No. 5,244,651) describe a method of desensitizing hypersensitive dentin comprised of treating teeth with a colloid produced by mixing a salt of a polyvalent metal and a polyol phosphate. The useful polyvalent metals. . . hydroxide is not water-soluble and thus is not mentioned by the inventors as a polyvalent metal of utility in the tooth desensitizing methods of the invention.

SUMM [0015] Thus, there is a need for **oral** compositions and methods comprising compounds that can scavenge free radicals and thereby reduce or eliminate the potential effects of reactive oxygen species on the tissues of the **oral** cavity.

SUMM [0016] There is also a need for **oral** compositions and methods that can provide for increased **tooth** surface remineralization capacity by increasing the availability of phosphate ions.

SUMM [0017] There is also a need for **oral** compositions and methods that can scavenge free radicals in the **oral** cavity, while simultaneously providing for increased **tooth** surface remineralization capacity by increasing the availability of phosphate ions.

SUMM . . . compound in combination with one or more additional dentally therapeutic ingredients, such as anticaries agents, tartar control agents, antiplaque agents, antimicrobial agents,

antigingivitis agents, desensitizing agents, and combinations thereof.

SUMM . . radical scavenging benefit as described above, while simultaneously providing at least one additional therapeutic benefit for the tissues of the oral cavity.

SUMM . . . that contain a stable source of ascorbic acid that does not deteriorate in the package prior to use in the oral cavity.

SUMM . . . a need for stable dental compositions that provide a bioactive source of ascorbic acid upon contact with tissues of the **oral** cavity.

SUMM . . . of the present invention are directed to compositions and methods comprising compounds that can scavenge free radicals present in the **oral** cavity, such as on tissue surfaces in the

oral cavity, and thereby reduce or eliminate the potential effects of reactive oxygen species on the tissues of the oral cavity. The compositions of the present invention include a precursor compound that generates a free radical scavenger when placed onto the tissue surface in an oral cavity. The free radical scavenger will in turn scavenge free radicals with which it comes in contact, thereby reducing the concentration of free radicals in the oral cavity. Reducing free radical scavengers in the oral cavity reduces the effects of conditions and diseases which result from the presence of free radicals in the oral cavity. [0023] Embodiments of the present invention are further directed to compositions and methods that can provide for increased tooth surface remineralization capacity by increasing the availability of phosphate ions. The compositions of the present invention include a phosphate precursor compound that can generate phosphate ions when placed onto the tissue surface in an oral cavity. The phosphate ions generated by the phosphate precursor compound combine with cations, such as calcium ions present in the oral cavity, to form calcium phosphates that precipitate on or within the tooth enamel or dentinal tubules, and accordingly, remineralize the tooth. Embodiments of the present invention are directed to compositions and methods that include compounds which scavenge free radicals in the oral cavity, while simultaneously providing for increased tooth surface remineralization capacity by increasing the availability of phosphate ions. . radical scavenging benefit as described above, while simultaneously providing at least one additional therapeutic benefit for the tissues of the oral cavity. According to the present invention the compositions optionally include one or more additional dentally therapeutic ingredients, such as anticaries agents, tartar control agents, antiplaque agents, antimicrobial agents, antigingivitis agents, desensitizing agents, and combinations thereof. [0026] The compositions of the present invention include the ingredients in the form of an oral rinse, a mouthwash, a dentifrice with or without abrasives, toothpastes, creams, gels and other topical formulations well known to those skilled in the art. . source of ascorbic acid that retains its potency and does not deteriorate in the package prior to use in the oral cavity. Further embodiments of the present invention provide stable dental compositions that include a bioactive source of ascorbic acid upon contact with tissues of the oral cavity. acceptable carrier, together with an optional auxiliary therapeutic ingredient, to prevent or cure various disease processes or symptoms of the oral cavity associated with the presence of free radicals. According to this aspect of the present invention, the composition including the ascorbyl phosphate is contacted with the tissue of the oral cavity. The ascorbyl phosphate generates ascorbic acid that then scavenges free radicals present on the tissue surface within the oral cavity, thereby reducing the concentration of free radicals present in the oral cavity. A particularly preferred ascorbyl phosphate is ascorbyl-2-phosphate. . of the present invention includes a method of therapeutically treating an individual afflicted with a disease or condition in the oral cavity associated with the presence of free radicals. The method includes contacting tissue within the oral cavity with a composition including a therapeutically effective amount of a free radical scavenging compound or a free radical scavenging precursor compound in a manner to reduce the concentration of free radicals within the oral cavity. According to one aspect of the present invention, the composition is contacted with the tissue within the oral cavity for a period of time sufficient to reduce the concentration of free radicals. According to certain embodiments, the composition. . . The free radical scavenging precursor compound

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generates a free radical scavenging compound that then scavenges free radicals present within the **oral** cavity.

SUMM [0030] In addition, the preferred ascorbyl phosphate compounds described herein display a surprising degree of adhesion to **oral** tissue including **tooth** enamel surface. Adhesion or attachment to the **tooth** enamel surface can prolong the effective duration of ascorbic acid and phosphate ion release into saliva by endemic phosphatase enzyme.

SUMM [0031] The term "topical" shall be used in this disclosure to mean applied to the surface of the intended target oral tissue, but shall also include oral tissue subsurfaces as a result of penetration of all or part of the inventive composition through said surface. For example, topical application of the inventive composition to the tooth enamel surface shall also include the underlying tooth structure (dentin, pulp, etc) that may become exposed to the composition by way of penetration through intact tooth enamel, or alternatively through the temporary exposure of such underlying oral tissue structure during a dental procedure.

SUMM [0033] According to certain preferred embodiments of the present invention, a topical **oral care** composition is provided which includes a free radical scavenging precursor compound in combination with orally acceptable carriers and optionally, therapeutically. . . A preferred free radical scavenging precursor compound is the family of ascorbyl phosphate compounds. The composition is placed within the **oral** cavity in contact with tissue within the **oral** cavity for a period of between about 5 minutes and about 60 minutes.

SUMM [0034] The addition of ascorbyl phosphates and their salts, such as the trisodium salt of ascorbyl-2-monophosphate, to toxicologically acceptable oral carriers results in useful oral care compositions that may be used to counteract tooth decay, prevent tooth stain accumulation and assist in the regenerative process of periodontal tissues.

SUMM . . . I, in order that biologically viable phosphate ions are immediately released into salivary solution upon contact with tissue in the oral cavity or the ascorbyl phosphate compound with phosphatase enzymes in the oral cavity. Biological viability may include participation in calcium phosphate formation and precipitation. Both the ascorbic acid and phosphate moieties of the inventive compositions become biologically viable after contact with the oral cavity.

SUMM [0038] The D-ascorbic acid form of ascorbyl phosphate may also have utility in certain **oral** applications, where only free radical scavenging is desired and not other biological functions (where the L-ascorbic acid is the only. . .

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. free radical scavenging precursor compound, such as those compounds of formula I, to one or more tissue surfaces in the oral cavity. Orally acceptable carriers include dosage forms such as toothpastes (dentifrices), gels, mouthwashes, rinses, chewing gums, lozenges, floss, interdental stimulating sticks, denture adhesives, buccal patches, tooth balms, dental tray-administered gels or pastes, sprays, chewable objects (such as an animal chew toy comprising rawhide as a carrier), food or feed coatings, topical dressings, or tooth varnishes. The orally acceptable carrier may also be administered to the oral cavity by means of or as part of an assembly or device, such as a dental tray, plastic strip, buccal patch, gingival retraction cord, or curable restorative material (such as a temporary cement or free-radically polymerized tooth composite). Oral acceptable carriers or delivery means for ascorbyl phosphate, other than those listed here, are known to those skilled in the.

. . . forms of calcium phosphate during use. Alternatively, the source of calcium ions may be saliva or saliva-coated surfaces in the  ${\bf oral}$  cavity. Compositions containing both an ascorbyl phosphate

ester and a calcium ion source may have utility in the remineralization of tooth enamel, and may be useful in the reversal of such early stage oral hard tissue disease processes such as primary root caries lesions. In one embodiment, the calcium ion source may be an. . . from one another to avoid mixing or contact with one another until the point of use or application to the oral cavity. A particularly useful package for this embodiment is a dual-chambered syringe with an attached static mixer assembly, whereby a. . . tool is also contemplated. In yet another embodiment, the calcium ion source may be found in saliva or on an oral cavity surface, whereby the mixing of an ascorbyl phosphate mixture with calcium ions occurs in situ, that is, on one or more oral cavity surfaces.

SUMM

. . . monofluorophosphate, stannous fluoride, amine fluorides, and other fluoride containing compounds capable of increasing the resistance of mineralized tissues in the **oral** cavity to caries formation (tooth decay). Anticaries agents may be included in the ascorbyl phosphate compositions at concentrations of from about 0.1% to about 4%. . .

SUMM

. . . may be employed in the ascorbyl phosphate compositions to assist in the reduction or prevention of tartar formation on the **teeth**. Useful tartar control agents include the sodium and potassium salts of pyrophosphate, tripolyphosphate, and polyphosphates, as well as other calcium. . .

SUMM [0059] Antimicrobial Agents

SUMM

[0060] In order to reduce or eliminate microorganisms responsible for oral diseases such as gingivitis, periodontitis, caries, and halitosis, an antimicrobial agent may be included in the inventive ascorbyl phosphate compositions. Such compounds are well known in the art, and include triclosan, chlorhexidine (and its salts), cetylpyridinium chloride, and essential oils including menthol, eucalyptol, thymol and methyl salicylate. Antimicrobial agents may be included in the ascorbyl phosphate compositions at concentrations between about 0.01% and about 2% by weight of. .

SUMM SUMM [0061] Tooth Desensitizing Agents
[0062] While the ascorbyl phosphate compounds described herein may also exhibit activity as tooth desensitizers, due to the release of phosphate ions into salivary solution upon contact with the oral cavity (thus encouraging tooth remineralization resulting from the precipitation of calcium phosphate at the tooth surface), it may be advantageous to add a supplementary tooth desensitizer such as potassium nitrate, potassium citrate, or strontium chloride hexahydrate in order to further alleviate tooth sensitivity. Such supplementary tooth desensitizers may be included in the ascorbyl phosphate compositions at a concentration of from about 0.1% by weight to about 10% by weight of the composition. Potassium nitrate is the preferred supplementary tooth desensitizer and is included in the composition at a concentration of

SUMM

. . . The ascorbyl phosphate compositions, together with any auxiliary active ingredients, may be in the form of (or delivered to the oral cavity by means of) a toothpaste (dentifrice), gel, mouthwash, chewing gum, lozenge, floss, interdental stimulating stick, denture adhesive, buccal patch, tooth balm, dental tray-administered gel or paste, spray, chewable object (such as an animal chew toy comprising rawhide as a carrier), food or feed coatings, topical dressing, or tooth varnish.

from about 3% to about 6% by weight of.

SUMM

chewing, swabbing, adhering or otherwise applying said compositions to one or more oral tissue surfaces. Application may also be made by placing an ascorbyl phosphate ester containing composition, for instance a gel, into a dental tray and attaching the tray to the maxillary (upper) and/or mandibular (lower) arch of teeth so that the teeth make contact with the gel inside the tray.

[0071] Compounds of formula I may also be added to other types of

DETD

oral care compositions, as well as certain types of foodstuffs, including, but not limited to, chewing gum, dental floss, tooth whitening gels and pastes, breath sprays, buccal patches, medicament delivery strips, and lozenges. Furthermore, any device or carrier for delivery of a compound of formula I to hard and/or soft tissue surfaces in the oral cavity is contemplated have utility as a delivery system or device for the compositions, and in the practice of the. . .

DETD . . . of a phosphatase enzyme inhibitor, such as a fluoride ion source, in the compositions of the present invention. Other auxiliary oral care ingredients, such as those employed for tartar control, tooth bleaching or whitening, halitosis elimination or prevention, and microbial control, may also be included. Also, one or more ingredients for. . . the compound of formula I in a fashion so as to keep it in intimate or close proximity to the tooth or oral mucosal surface.

DETD . . . for use as one part compositions (whereby no mixing of components is necessary prior to applying the composition to the **oral** cavity). Suitable packages include syringes, tubes, bottles, jars, and unit dose packages, to name a few.

DETD . . . compositions (whereby two separately packaged components are combined to form a single component mixture just prior to application to the **oral** cavity) may be utilized. Two part compositions may be packaged by placing one of the components of the system in. . . mixer assembly. The mixture that emerges from the end of the static mixer assembly is preferably applied directly to the **oral** cavity, rather than being stored for an extended period of time.

DETD . . . or multi-part systems may be applied in sequence, whereby one separately packaged component is applied to a surface of the oral cavity, followed by the application (to the same oral cavity surface) of a second separately packaged component to the oral cavity, etc. Mixing of the two or more components is thus accomplished in situ, rather than prior to application.

DETD [0076] Method of Preventing **Tooth** Sensitivity Associated with Peroxide **Tooth** Whitening

DETD [0077] Most tooth whitening compositions that are capable of eliminating or reducing both extrinsic and intrinsic tooth staining contain an oxidizing compound. Typically, the oxidizing compound is either hydrogen peroxide, or a precursor to hydrogen peroxide, such. . . in enamel or exposed root surfaces), thus reaching vital pulp tissue within 15 minutes from initial contact of the peroxide tooth whitening composition on the tooth surface. It is speculated that the presence of peroxide in the pulp chamber is one of the major contributors to tooth sensitivity associated with such tooth whitening procedures.

DETD [0078] A particularly useful application of the inventive ascorbyl

[0078] A particularly useful application of the inventive ascorbyl phosphate compositions is for alleviating or preventing the tooth sensitivity often associated with the use of peroxide-containing tooth whitening compositions. Upon contact with a tooth surface that has been treated with a peroxide-containing tooth whitening composition, the ascorbyl phosphate compositions provide a source of ascorbic acid upon hydrolysis by phosphatase enzymes present in the oral cavity. Ascorbic acid is known to be a powerful free-radical scavenger. While not wishing to be bound by any particular theory, release of ascorbic acid from ascorbyl phosphate applied to the oral cavity may reduce the likelihood of pulp tissue damage by scavenging free-radical degradation products of hydrogen peroxide, such as the. . . after hydrolysis of the ascorbyl phosphate molecule, in that free phosphate ion is released into salivary solution and at the tooth surface, thus creating conditions that are highly conducive to formation (typically by precipitation) of calcium phosphate crystals within the dentinal tubules. Blockage of the dentinal tubules is known to decrease tooth sensitivity by reducing the likelihood of fluid movement

within the tubules caused by external stimuli, such as heat, cold, and.

DETD [0079] A preferred method of reducing or eliminating the **tooth** sensitivity associated with peroxide-based **tooth** whitening procedures comprises the sequential steps of

DETD [0080] 1. Contacting a **tooth** surface or **tooth** surfaces with a peroxide-containing **tooth** whitening composition for a period of time in order to effect **tooth** whitening,

DETD [0081] 2. Contacting the same **tooth** surface or **tooth** surfaces with a composition comprising a compound of formula I, such as an ascorbyl phosphate

DETD [0082] Optionally, the ascorbyl phosphate compositions of the above method may contain other ingredients commonly employed in oral care formulations, such as humectants, thickeners, preservatives, foaming agents, solubilizers, adherence-enhancing agents, phosphatase enzyme inhibitors, antimicrobial agents, anticaries agents, tartar control agents, tooth desensitizing agents, sweeteners, and flavorants.

DETD . . . the ascorbyl phosphate in the method above can be a liquid, gel, paste, cream, stick, chewing gum, or any other oral care vehicle as would be well known to those skilled in the art. The compositions of the above method may be applied or positioned into close proximity with an oral cavity surface by rinsing, brushing, spraying, or chewing. An oral cavity surface may be the surface of a tooth, the oral mucosal, the tongue, or even a surface temporarily exposed during a dental surgical procedure, such as a root canal or cavity excavation. Another means of applying the compositions of the above method onto an oral cavity surface is by placing the composition in a dental tray, on a strip, or on a patch, and then placing said dental tray, strip or patch in the oral cavity, preferably in direct contact with the oral cavity surfaces to be treated.

DETD . . . have been prepared that demonstrate antioxidant activity when used as a denture adhesive to temporarily affix a denture to an **oral** mucosal surface. One example of such a denture adhesive is provided in the table below.

Petrolatum 31.259
Mineral Oil 14.271

Ascorbyl-2-phosphate, Na/Ca. . .

CLM What is claimed is:

1. An **oral care** composition comprising (a) an orally acceptable carrier, and (b) an ascorbyl-2-phosphate compound having the following structure, or a sodium or. . .

. The composition of claim 1 which optionally includes one or more of an anticaries agent, a tartar control agent, an **antimicrobial** agent, and a desensitizing agent.

. The composition of claim 1 further including an ingredient promoting the adherence of the compound of formula I to the **tooth** or **gums**.

IT 23313-12-4 30784-77-1 109113-30-6 125913-31-7, Rovimix Stay-C 35 134885-32-8 143567-34-4 (topical oral care compns. contg. ascorbyl phosphate)

L14 ANSWER 4 OF 7 USPATFULL

ACCESSION NUMBER: 2002:88005 USPATFULL

TITLE: Cosmetic skin care compositions containing cumic

alcohol

INVENTOR(S): Carson, Robert, Rahway, NJ, United States
Patel, Krupa, Edison, NJ, United States

Pillai, Sreekumar, Wayne, NJ, United States

Granger, Stewart Paton, Paramus, NJ, United States Lange, Beth Anne, Appleton, WI, United States Unilever Home & Personal Care (USA), division of

Conopoco, Inc., Greenwich, CT, United States (U.S.

corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 6375961 B1 20020423 APPLICATION INFO.: US 2000-597053 20000620 (9)

NUMBER DATE

PRIORITY INFORMATION: US 1999-141636P 19990630 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: GRANTED

PRIMARY EXAMINER: Williamson, Michael A.

LEGAL REPRESENTATIVE: Plotkin, Ellen

NUMBER OF CLAIMS: 10 EXEMPLARY CLAIM: 1

PATENT ASSIGNEE(S):

NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)

LINE COUNT: 526

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . materials for various skin benefits such as sunscreen

(J010182416), anti-oxidant (J02204495), whitening agent (J06256150), reduction of contact dermatitis (J04356423, J04356424),

antimicrobial cosmetic preservative (J62181202, J09202712),

bathing composition for dry skin (J09002939), acne cream (CN1136431) and

hair growth (WO9522957).

SUMM . . . weight of the composition. Exemplary thickeners are cross-linked polyacrylate materials available under the trademark Carbopol from the B.F. Goodrich Company. Gums may be employed such as xanthan, carrageeran, gelatin, karaya, pectin and locust beans gum. Under certain circumstances the thickening function may be

gum. Under certain circumstances the thickening function may be accomplished by a material also serving as a silicone or emollient. For instance, silicone gums in excess of 10 centistokes and esters

such as glycerol stearate have dual functionality.

50-81-7, Ascorbic acid, biological studies 50-99-7, Glucose, biological studies 57-50-1, Sucrose, biological studies 59-23-4, Galactose, biological studies 63-42-3, Lactose 536-60-7, Cumic alcohol 1330-84-3 3416-24-8, Glucosamine 25395-66-8, Ascorbyl stearate 82643-14-9, Glucose glutamate 108910-78-7, Magnesium Ascorbyl phosphate 110632-98-9, Sodium Ascorbyl monophosphate 161436-56-2, Ascorbyl tetraisopalmitate 317351-67-0, Glucose phosphate

(cosmetic compns. contg. cumic alc.)

L14 ANSWER 5 OF 7 USPATFULL

ACCESSION NUMBER: 2000:109786 USPATFULL

TITLE: Compounds and their combinations for the treatment of

influenza infection

INVENTOR(S): Jones, Dean P., Decatur, GA, United States

Furukawa, Satoru, Tokyo, Japan

PATENT ASSIGNEE(S): Nutri-Quest, Inc., Chesterfield, MO, United States

(U.S. corporation)

Emory University, Atlanta, GA, United States (U.S.

corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 6107281 20000822 APPLICATION INFO.: US 1999-339629 19990624 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 1998-5747, filed on 12 Jan

1998, now patented, Pat. No. US 6013632

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NUMBER DATE
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                        US 1997-35087P 19970113 (60)
US 1997-35088P 19970113 (60)
US 1997-34496P 19970113 (60)
US 1997-35417P 19970113 (60)
PRIORITY INFORMATION:
DOCUMENT TYPE:
                        Utility
FILE SEGMENT:
                        Granted
                        Nutter, Nathan M.
PRIMARY EXAMINER:
                        Pratt, John S., Gray, Bruce D.Kilpatrick Stockton LLP
LEGAL REPRESENTATIVE:
NUMBER OF CLAIMS:
EXEMPLARY CLAIM:
LINE COUNT:
                        1206
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       . . . form of chemical carcinogens is typically electrophiles, which
       can be detoxified by reactions catalyzed by GSH S-transferases.
       Administration of large oral dosages of GSH to rats with liver
       cancer results in substantial regression of the liver tumor. As noted
       above, GSH.
          . . of the epithelial cells so that supply of these compositions at
SUMM
       relevant concentrations to the apical surface of the nasal, oral
       and upper respiratory epithelia can have the same effect by inhibiting
       protease activation of influenza virus.
SUMM
               which are a primary site of initial infection in vivo. Thus,
       preparation of these compositions for direct delivery to the
       oral, nasal and respiratory epithelia, such as lozenge,
       oral rinse or nasal spray, can be used to prevent influenza
       infection. Other thiols and antioxidants can also have this effect.
        in risk of infection in humans and in veterinary or domestic animals.
       Preparations for supply of these compositions directly to oral
       , nasal and airway epithelia may also protect against other viral
       infections (e.g., common cold). In principle, vaginal or rectal
       suppositories,. .
            . acids and bases to adjust the pH; (2) other tonicity imparting
SUMM
       agents such as sorbitol, glycerin and dextrose; (3) other
       antimicrobial preservatives such as other parahydroxy benzoic
       acid esters, sorbate, benzoate, propionate, chlorbutanol, phenylethyl
       alcohol, benzalkonium chloride, and mercurials; (4) other viscosity
       imparting agents such as sodium carboxymethylcellulose, microcrystalline
       cellulose, polyvinylpyrrolidone, polyvinyl alcohol and other
       gums; (5) suitable absorption enhancers; (6) stabilizing agents
       such as antioxidants, like bisulfite and ascorbate, metal chelating
       agents such as sodium.
         . . the above-indicated conditions. In one preferred regimen, such
SUMM
       dosages are administered to each patient by either nasal spray or by
       oral lozenge. It will be understood, however, that the specific
       dose level and frequency of dosage for any particular patient may.
         . . is to prevent extracellular activation of the virus, a process
DETD
       which can be achieved by supply of GSH to the oral, nasal and
       upper airway epithelium by oral rinse, lozenge, nasal spray or
       aerosolizer.
CLM
       What is claimed is:
         virus, by administering to a patient in need of such treatment an
       effective amount of a pharmaceutical composition suitable for
       oral, nasal or rectal administration comprising: (a) a compound
       selected from the group consisting of glutathione and glutathione
       disulfide, or a pharmaceutically acceptable salt thereof, and (b) a
       pharmaceutically acceptable carrier suitable for oral, nasal
       or rectal administration, said composition useful in preventing or
       treating of influenza virus infection.
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616-91-1P, N-Acetylcysteine

70-18-8P, Glutathione, biological studies

23313-12-4P, Ascorbic acid 2-phosphate 27025-41-8P, Glutathione

IT

disulfide

(compds. and pharmaceuticals for treatment of influenza virus infection)

L14 ANSWER 6 OF 7 USPATFULL

ACCESSION NUMBER: 2000:4794 USPATFULL

TITLE: Compounds and their combinations for the treatment of

influenza infection

INVENTOR(S): Jones, Dean P., Decatur, GA, United States

Furukawa, Satoru, Tokyo, Japan

PATENT ASSIGNEE(S): Emory University, Atlanta, GA, United States (U.S.

corporation)

Nutri-Quest, Inc., Chesterfield, MO, United States

(U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6013632		20000111	
APPLICATION INFO.:	US 1998-5747		19980112	(9)

NUMBER DATE

PRIORITY INFORMATION: US 1997-35087P 19970113 (60)
US 1997-35088P 19970113 (60)
US 1997-34496P 19970113 (60)
US 1997-35417P 19970113 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: Nutter, Nathan M. LEGAL REPRESENTATIVE: Kilpatrick Stockton LLP

NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
LINE COUNT: 1216

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . form of chemical carcinogens is typically electrophiles, which can be detoxified by reactions catalyzed by GSH S-transferases.

Administration of large oral dosages of GSH to rats with liver cancer results in substantial regression of the liver tumor. As noted above, GSH. . .

SUMM . . . of the epithelial cells so that supply of these compositions at relevant concentrations to the apical surface of the nasal, **oral** and upper respiratory epithelia can have the same effect by inhibiting protease activation of influenza virus.

SUMM . . . which are a primary site of initial infection in vivo. Thus, preparation of these compositions for direct delivery to the oral, nasal and respiratory epithelia, such as lozenge, oral rinse or nasal spray, can be used to prevent influenza infection. Other thiols and antioxidants can also have this effect. . . in risk of infection in humans and in veterinary or domestic animals. Preparations for supply of these compositions directly to oral , nasal and airway epithelia may also protect against other viral infections (e.g., common cold). In principle, vaginal or rectal suppositories, . .

SUMM . . . acids and bases to adjust the pH; (2) other tonicity imparting agents such as sorbitol, glycerin and dextrose; (3) other antimicrobial preservatives such as other parahydroxy benzoic acid esters, sorbate, benzoate, propionate, chlorbutanol, phenylethyl alcohol, benzalkonium chloride, and mercurials; (4) other viscosity imparting agents such as sodium carboxymethylcellulose, microcrystalline cellulose, polyvinylpyrrolidone, polyvinyl alcohol and other gums; (5) suitable absorption enhancers; (6) stabilizing agents such as antioxidants, like bisulfite and ascorbate, metal chelating agents such as sodium. . .

SUMM . . . the above-indicated conditions. In one preferred regimen, such

dosages are administered to each patient by either nasal spray or by oral lozenge. It will be understood, however, that the specific dose level and frequency of dosage for any particular patient may.

is to prevent extracellular activation of the virus, a process DETD which can be achieved by supply of GSH to the oral, nasal and upper airway epithelium by oral rinse, lozenge, nasal spray or aerosolizer.

CLM What is claimed is:

- 1. A pharmaceutical composition suitable for oral, nasal or rectal administration comprising (a) glutathione, or a pharmaceutically acceptable salt thereof; and (b) a pharmaceutically acceptable carrier suitable for oral, nasal or rectal administration, said composition useful in preventing or treating influenza virus infection.
- 1, which is in a form selected from the group consisting of a lozenge, a cough drop, a tablet, an oral rinse, a drinking solution, nasal drops, a nasal spray, an oleaginous suspension, and a suppository.
- 5. A pharmaceutical composition suitable for oral, nasal or rectal administration comprising (a) glutathione disulfide, or a pharmaceutically acceptable salt thereof; and (b) a pharmaceutically acceptable carrier,.
- 70-18-8P, Glutathione, biological studies 616-91-1P, N-Acetylcysteine IT23313-12-4P, Ascorbic acid 2-phosphate 27025-41-8P, Glutathione

(compds. and pharmaceuticals for treatment of influenza virus infection)

L14 ANSWER 7 OF 7 COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 1999:22127 NLDB

TITLE:

1998 FOOD ADDITIVE SUMMARY.

SOURCE:

Food Chemical News, (25 Jan 1999) Vol. 40, No. 49.

ISSN: 0015-6337.

PUBLISHER:

Food Chemical News, Inc.

DOCUMENT TYPE: Newsletter LANGUAGE: English

WORD COUNT:

20496

CHLORINE DIOXIDE. Amended [section] 173.300 to allow the safe use of chlorine dioxide as an antimicrobial agent in water used to wash certain fruits and vegetables intended for human consumption. National

Food Processors Association petition filed.

maleate, and methylvinyl cyclosiloxane as optional polymerization inhibitors; and (3) 5-chloro-2-methyl-4-iso-thiazolin-3-one and 2-methyl-4-isothiazolin-3-one mixtures, optionally containing magnesium nitrate, as an antimicrobial agent for emulsion-based silicone coating formulations. Dow Corning petition filed Feb. 12, 1993 (Feb. 15, 1993, Page 69). Amended July.

2,4,4'-TRICHLORORO-2-HYDROXYDIPHENYL ETHYL. To clear use as an antimicrobial agent in the manufacture of polyvinyl chloride gloves for food-contact use. Phoenix Medical Technology, Nov. 6, 1991 (Nov. 11, 1991,.

NEOMYCIN SULFATE ORAL SOLUTION. Amended [section] 520.1485 to provide for revised withdrawal time of 30 days for cattle and goats and 20 days for swine and sheep, for oral solution as a drench and in drinking water for the treatment and control of colibacillosis. Abbreviated NADA from Phoenix Scientific.

STREPTOMYCIN ORAL SOLUTION. Amended [section] 520 to provide for the use of streptomycin oral solution in drinking water for the treatment of nonspecific infectious enteritis in chickens and for the treatment of bacterial enteritis. . .

SULFADIMETHOXINE **ORAL** SOLUTION AND SOLUBLE POWDER. Amended [section]520.2220a to provide for use of sulfadimethoxine soluble powder for use in drinking water as a drench and for use of the **oral** solution in drinking water as a drink, for treatment of various diseases in chicken, meat-producing turkeys, and dairy calves, dairy. . .

CHEMICALS . . . [section]173.315 to provide for the safe use of a mixture of peroxyacetic acid, hydrogen peroxide and 1-hydroxyethylidene-1,1-diphosphonic acid as an **antimicrobial** agent to wash or assist in the lye peeling of fruits and vegetables that are not raw agricultural commodities without. . .

PEROXYACETIC ACID, ACETIC ACID AND HYDROGEN
PEROXIDE. To amend [section]178.315 to clear use to control microbial growth in water contacting fruits and vegetables. Ecolab Inc., July 13, 1995 (July 17, 1995, Page 26).

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